LISTING OF CLAIMS

- 1. (currently amended): A method for selective isolation and culturing of tissue specific progenitor cells or stem-like cells from a tissue biopsy comprising culturing said tissue biopsy in culture medium comprising serum in a volume/volume (v/v) concentration the presence of at least 25% serum relative to the amount of culture medium.
- 2. (currently amended): A method according to claim 1, wherein the serum concentration is between about 25% to about 70%.
- 3. (currently amended): A method according to claim 1, wherein the serum <u>concentration</u> is between about 30% to about 50%.
- 4. (currently amended): A method according to claim 1, wherein the serum <u>concentration</u> is between about 30%.
- 5. (currently amended): A method according to any one of claims claim 1, to 4 wherein the culture medium is selected from the group consisting of Synthetic Oviductal Fluid (SOF), Modified Eagle's Medium (MEM), Dulbecco's Modified Eagle's Medium, (DMEM), RPMI 1640 Medium, F-12 Medium, Iscove's Modified Dulbecco's Medium (IMDM), Alpha Medium and McCoy's Medium.
- 6. (original): A method according to claim 5, wherein the serum is selected from the group consisting of allogeneic serum, autologous serum and xenogeneic serum.
- 7. *(original):* A method according to claim 6, wherein the serum is heat-inactivated autologous serum.
- 8. (currently amended): A method according to any one of claims claim 1 to 7, wherein the culture medium further comprising growth factors, co-factors, salts, or antibiotics.
- 9. (currently amended): A method according to claim 1, further -for tissue-specific progenitor cells or stem cell-like cells from a tissue biopsy comprising the step of (i) obtaining a tissue biopsy from an animal; (ii) culturing said tissue biopsy in tissue culture medium comprising at least 25% serum; and (iii) replacing about 50% of the culture medium including serum about every 48 hours.

- 10. (currently amended): A method according to any one of claims claim 1-to-9, wherein the tissue biopsy is biopsies are cultured in the presence of a feeder cell layer.
- 11. (original): A method according to claim 10, wherein the feeder cell layer comprises cultured autologous cells.
- 12. (currently amended): A method according to any one of claims claim 1-to 11, wherein the tissue biopsy is biopsies are obtained from a mammal mammalian animal.
- 13. (currently amended): A method according to claim 12, wherein the <a href="mammal mammal m
- 14. (currently amended): A method according to claim 12, wherein the <u>mammal tissue biopsies</u> are isolated from is an ungulate selected from the group consisting of domestic or wild bovid, ovid, cervid, suid, equid and camelid.
- 15. (currently amended): A method according to claim 12, wherein the <u>mammal is tissue</u> biopsies are isolated from a human subject.
- 16. (currently amended): A method according to any one of claims claim 12-to-15, wherein the tissue biopsy is biopsies are obtained from an organ selected from the group consisting of skin, lung, pancreas, liver, stomach, intestine, heart, a reproductive organ[[s]], bladder, kidney, urethra or and other urinary tissue or organ[[s]].
- 17. (currently amended): A method according to claim 16, wherein the tissue biopsy is biopsies are obtained from fetal tissue.

- 18. (currently amended): A method according to claim 16 [[17]], wherein the tissue biopsy is biopsies are obtained from adult tissue.
- 19. (currently amended): An isolated tissue-specific progenitor cell or stem cell-like cell obtained by a method according to any one of claims claim 1-to 18.
- 20. (original): An isolated tissue-specific progenitor cell according to claim 19, wherein the cell is a mesenchymal connective tissue-derived stem cell.
- 21. (original): An isolated mesenchymal connective tissue-derived stem cell according to claim 20, wherein the cell has the capacity to be induced to differentiate to form at least one differentiated cell type of mesodermal, ectodermal, or endodermal origin.
- 22. (currently amended): A cell according to claim 20 or claim 21, wherein said cell that is derived from a non-embryonic organ or tissue of a mammal.
- 23. (currently amended): A cell according to any one of claims claim 20 to 22, wherein the cell that has the capacity to be induced to differentiate into an form cells selected from the group consisting of osteoblast, a chondrocyte, an adipocyte, a fibroblast, a bone marrow stromal cell, a skeletal muscle cell, a smooth muscle cell, a cardiac muscle cell, an ocular cell, an endothelial cell, an epithelial cell, a hepatic cell, a pancreatic cell, a hematopoietic cell, a glial cell, a neuronal cell, or and an oligodendrocyte cell type.
- 24. *(original)* A cell according to claim 22, wherein the organ or tissue is selected from the group consisting of bone marrow, muscle, brain, umbilical cord blood and placenta.
- 25. (currently amended): A cell according to <u>claim any one of claims-22 to 24</u>, wherein the mammal is a human.
- 26. (currently amended): A cell according to <u>claim</u> 21 any one of claims 22 to 25, wherein <u>said</u> differentiation is induced in vivo or ex vivo.
- 27. (currently amended): A cell according to any one of claims claim 19 to 26, wherein the cell constitutively expresses oct4 and high levels of telomerase.

28. (original): An isolated mesenchymal connective tissue-derived stem cell as deposited under the Budapest Treaty at the Deutsche Sammlung Von Mikroorganismen und Zellkulturen GmbH (DSMZ), Germany on 27 October 2004, under accession number DSM ACC 2697.

- 29. (currently amended): A method of <u>producing ereating</u> a normal non-human animal comprising the steps of:
 - (a) introducing a cell according to any one of claims claim 19 to 28 into a blastocyst;
 - (b) implanting the blastocyst of (a) into a surrogate mother; and
 - (c) allowing the <u>blastocyst to develop into a pup[[s]]</u> to develop and the pup to be born.
- 30. (original): A method according to claim 29, wherein the normal non-human animal is a chimeric animal.
- 31. (currently amended): A composition comprising a population of cells according to any one of claims claim 19 to 28 and a culture medium, wherein the cell population can expand in the culture medium expands the cells.
- 32. (currently amended): A composition according to claim 31, wherein the culture medium comprises epidermal growth factor (EGF) and platelet derived growth factor (PDGF).
- 33. *(currently amended)*: A composition according to claim 32, wherein the culture medium further comprises leukemia inhibitory factor (LIF).
- 34. *(currently amended)*: A composition comprising a population of fully or partially purified cells according to any one of claims claim 19 to 28 or progeny thereof.
- 35. (currently amended): A composition according to claim 34, wherein the progeny <u>cells</u> have the capacity to be further differentiate[[d]].
- 36. *(currently amended)*: A composition according to claim 34, wherein the progeny <u>cells</u> have the capacity to terminally differentiate.

- 37. (currently amended): A composition according to claim 34, wherein the progeny <u>cells</u> are of the-osteoblasts, chondrocytes, adipocytes, fibroblasts, marrow stromal <u>cells</u>, skeletal muscle <u>cells</u>, smooth muscle <u>cells</u>, cardiac muscle <u>cells</u>, ocular <u>cells</u>, endothelial <u>cells</u>, epithelial <u>cells</u>, hepatic <u>cells</u>, pancreatic <u>cells</u>, hematopoietic <u>cells</u>, glial <u>cells</u>, neuronal <u>cells</u> or oligodendrocytes <u>cell type</u>.
- 38. (currently amended): A method for isolating and propagating [[a]] mesenchymal connective tissue-derived stem cells comprising the steps of:
 - (a) obtaining a tissue biopsy from a mammal;
 - (b) establishing a population of adherent cells by culturing said biopsy in medium that comprises the presence of at least 25% serum (v/v);
 - (c) recovering said mesenchymal connective tissue-derived stem cells <u>from the</u> <u>population of (b)</u>; and
 - (d) culturing the mesenchymal connective tissue-derived stem cells under expansion conditions to produce an expanded cell population.
- 39. (currently amended): An expanded eell population of mesenchymal connective tissuederived stem cells obtained by a method according to claim 38.
- 40. (currently amended): A method for inducing differentiation of differentiating mesenchymal connective tissue-derived stem cells ex vivo, comprising the steps of:
 - (a) obtaining a tissue biopsy from a mammal;
 - (b) establishing a population of adherent cells by culturing said biopsy in the presence of medium that comprises at least 25% serum (v/v);
 - (c) recovering said mesenchymal connective tissue-derived stem cells from the population of (b);
 - (d) culturing the mesenchymal connective tissue-derived stem cells under expansion conditions to produce an expanded cell population; and
 - (e) culturing the <u>expanded propagated</u> cells in the presence of desired differentiation factors or agents.

thereby inducing said differentiation of said mesenchymal connective tissue-derived stem cells.

- 41. (currently amended): A method according to claim 40, wherein the differentiation factors or agents are selected from the group consisting of (a) basic fibroblast growth factor (bFGF), (b) vascular endothelial growth factor (VEGF), (c) dimethylsulfoxide, (DMSO) (d) isoproterenol, (e) fibroblast growth factor-4, (FGF4) and (f) hepatocyte growth factor, (HGF) and a combination of any of (a)-(f).
- 42. (currently amended): A method according to claim 41, wherein the differentiated cells obtained by said method are [[is]] ectodermal, mesodermal or endodermal cells.
- 43. (currently amended): A method according to claim 42, wherein the differentiated cells obtained by said method are is of the osteoblasts, chondrocytes, adipocytes, fibroblasts, bone marrow stromal cells, skeletal muscle cells, smooth muscle cells, cardiac muscle cells, ocular cells, endothelial cells, epithelial cells, hepatic cells, pancreatic cells, hematopoietic cells, glial cells, neuronal cells or oligodendrocytes.
- 44. (currently amended): A method for <u>inducing differentiation of differentiating</u> a mesenchymal connective tissue-derived stem cell in vivo, comprising the steps of:
 - (a) obtaining a tissue biopsy from a mammal;
 - (b) establishing a population of adherent cells by culturing said biopsy in the presence of medium that comprises at least 25% serum (v/v);
 - (c) recovering said mesenchymal connective tissue-derived stem cells <u>from the</u> <u>population of (b);</u>
 - (d) culturing mesenchymal connective tissue-derived stem cells under expansion conditions to produce an expanded cell population; and
- (e) administering the expanded cell population to a mammalian host, wherein said expanded cell-population of mesenchymal connective tissue-derived stem cells engraft is engrafted and differentiate differentiated in vivo into tissue specific cells, such that augment, reconstitute or provide for the first time in said host a the-function of a cell or organ that was defective or absent as a result of a disease or condition resulting from due to injury, a genetic disease, an acquired disease or an introgenic cause treatments, is augmented, reconstituted or provided for the first time.

1

- 45. (currently amended): A method according to claim 44, wherein the tissue specific cells are of the osteoblasts, chondrocytes, adipocytes, fibroblasts, bone marrow stromal cells, skeletal muscle cells, smooth muscle cells, cardiac muscle cells, ocular cells, endothelial cells, epithelial cells, hepatic cells, pancreatic cells, hematopoietic cells, glial cells, neuronal cells or oligodendrocytes cell type.
- 46. (currently amended): A method according to claim 44 or-elaim 45, wherein the mesenchymal connective tissue-derived stem cell undergoes self-renewal in vivo.
- 47. (currently amended): A method according any one of claims claim 44 to 46, wherein the cells are administered in conjunction with a pharmaceutically acceptable matrix.
- 48. (original): A method according to claim 47, wherein the matrix is biodegradable.
- 49. (currently amended): A method according to any one of claims claim 44 to 48, wherein administration is via-localized injection, systemic injection, parenteral administration, or al administration, or by intrauterine injection into an embryo.
- 50. (currently amended): A method according to claim 49, wherein <u>said</u> localized injection <u>administration</u> is via a <u>comprises</u> catheter <u>administration</u>.
- 51. (currently amended): A method according to any one of claims claim 44 to 50, wherein the disease or condition is selected from the group consisting of cancer, cardiovascular disease, metabolic disease, liver disease, diabetes, hepatitis, hemophilia, degenerative or traumatic neurological condition[[s]], autoimmune disease, genetic deficiency, connective tissue disorder[[s]], anemia, an infectious disease and transplant rejection.
- 52. (currently amended): A differentiated cell obtained by a method according to any one of claims claim 44 to 51.
- 53. (currently amended): A method of <u>treating treatment treating a disease or condition in a mammal that results in a defective or missing function of a cell, tissue or organ, the method comprising administering to <u>an animal a mammal</u> in need thereof a therapeutically effective amount of [[a]] cells according to claim 52.</u>

54. (currently amended): A method according to claim 55, wherein the treatment does not give rise to no-teratomas are formed in the subject animal.

- 55. (currently amended): A method of treatment treating a disease or condition in a mammal that results in defective or missing function of a cell, tissue, or organ, the method comprising administering to an animal a mammal in need thereof a therapeutically effective amount of mesenchymal connective tissue-derived stem cells or their progeny.
- 56. (currently amended): A method according to claim 55, wherein reduced or no pretreatment of the animal mammal is required for the treatment of said disease or condition.
- 57. (currently amended): A method according to claim 56, wherein the pretreatment comprises myeloablation by via-irradiation or chemotherapy.
- 58. (currently amended): A method according to claim 55, wherein a dose level of desired post immunosuppressive treatment of the mammal patient to which the cells were administered is reduced compared with traditional pharmacological immunosuppressive doses.
- 59. (currently amended): A method according to any one of claims claim 55 to 58, wherein the progeny cells have the capacity to be for further differentiation differentiated.
- 60. (currently amended): A method according to claim 59, wherein the progeny <u>cells</u> are terminally differentiated.
- 61. (currently amended): A method according to any one of claims claim 55 to 60, wherein the mesenchymal connective tissue-derived stem cells or their progeny are administered <u>locally</u>, via <u>localized injection</u>, systemically <u>injection</u>, parenterally <u>administration</u>, orally, or <u>by</u> intrauterine injection into an embryo.
- 62. (currently amended): A method according to claim 61, wherein <u>said local administration</u> localized injection comprises is via catheter administration.
- 63. (currently amended): A method according to any one of claims claim 55 to 62, wherein the cells are administered in conjunction with a pharmaceutically acceptable matrix.
- 64. (original): A method according to claim 63, wherein the matrix is biodegradable.

65. (currently amended): A method according to any one of claims claim 55 to 64, wherein the mesenchymal connective tissue-derived stem cells or their progeny alter the immune system to resist viral, bacterial or fungal infection.

- 66. (currently amended): A method according to any one of claims claim 55 to 64, wherein the mesenchymal connective tissue-derived stem cells or their progeny augment, reconstitute or provide for the first time in said host, a the function of a cell, tissue, or organ that is defective or absent as a result of due to a disease or condition resulting from injury, genetic disease, acquired disease or iatrogenic causetreatments.
- 67. (currently amended): A method according to claim 66, wherein the <u>defective</u> organ <u>or tissue</u> is selected from the group consisting of bone marrow, blood, spleen, liver, lung, intestinal tract, eye, brain, immune system, circulatory system, bone, connective tissue, muscle, heart, blood vessel[[s]], pancreas, central nervous system, peripheral nervous system, kidney, bladder, skin, epithelial appendage[[s]], breast <u>or</u> mammary gland[s], <u>adipose fat tissue</u>, <u>and mucosal surface including</u> oral mucosa, esophageal mucosa, vaginal <u>mucosa</u> or anal <u>mucosa</u>.
- 68. (currently amended): A method according to any one of claims claim 55 to 67, wherein the mesenchymal connective tissue-derived stem cells or their progeny undergo self-renewal in vivo.
- 69. (currently amended): A method according to claim 66, wherein the disease or condition is selected from the group consisting of cancer, cardiovascular disease, metabolic disease, liver disease, diabetes, hepatitis, hemophilia, a degenerative or traumatic neurological condition[[s]], autoimmune disease, genetic deficiency, a connective tissue disorder[[s]], anemia, an infectious disease and transplant rejection.
- 70. (currently amended): A method according to any one of claims claim 55 to 69, wherein the progeny cells are induced to differentiate[[d]] ex vivo or in vivo.
- 71. (currently amended): A method according to claim 70, wherein the progeny <u>cells</u> are selected from the group consisting of osteoblasts, chondrocytes, adipocytes, fibroblasts, <u>bone</u> marrow stromal <u>cells</u>, skeletal muscle <u>cells</u>, smooth muscle <u>cells</u>, cardiac muscle <u>cells</u>, ocular <u>cells</u>, endothelial <u>cells</u>, epithelial <u>cells</u>, hepatic <u>cells</u>, pancreatic <u>cells</u>, hematopoietic <u>cells</u>, glial <u>cells</u>, neuronal cells, and or oligodendrocytes.

72. (currently amended): A method according to any one of claims claim 55 to 71, wherein the mesenchymal connective tissue-derived stem cells or their progeny cells home to are engrafted in one or more organs in the host animal and are engrafted therein such that the defective function of said[[a]] cell, tissue or organ, defective due to injury, genetic disease, acquired disease or introgenic treatments, is augmented, reconstituted or provided for the first time.

73. (currently amended) A method according to claim 72, wherein the disease <u>or condition</u> is selected from the group consisting of cancer, cardiovascular disease, metabolic disease, liver disease, diabetes, hepatitis, hemophilia, <u>a</u> degenerative or traumatic neurological condition[[s]], autoimmune disease, genetic deficiency, <u>a</u> connective tissue disorder[[s]], anemia, <u>an</u> infectious disease and transplant rejection.

74. (currently amended): A method according to claim 72, wherein the <u>disease or condition</u> results from injury is ischemia or inflammation.

75. (currently amended): A method according to claim 72, wherein the <u>defective</u> organ <u>or tissue</u> is selected from the group consisting of bone marrow, blood, spleen, liver, lung, intestinal tract, eye, brain, immune system, circulatory system, bone, connective tissue, muscle, heart, blood vessel[[s]], pancreas, central nervous system, peripheral nervous system, kidney, bladder, skin, epithelial appendage[[s]], breast <u>or</u> mammary gland[s], <u>adipose fat-tissue</u>, <u>and mucosal-surface including-oral mucosa</u>, esophageal <u>mucosa</u>, vaginal <u>mucosa</u> and <u>or</u> anal <u>mucosa</u>.

76. (currently amended): A method according to any-one of claims claim 55to 75, wherein the mesenchymal connective tissue-derived stem cells or their progeny cells are genetically transformed as a result of which they are able to deliver a therapeutic agent to the host.

77. (currently amended): A therapeutic composition comprising mesenchymal connective tissue-derived stem cells and a pharmaceutically acceptable carrier, wherein the mesenchymal connective tissue derived stem cells are present in an amount effective to produce a tissue selected from the group consisting of bone marrow, blood, spleen, liver, lung, intestinal tract, eye, brain, immune system, bone, connective tissue, muscle, heart, blood vessel[[s]], pancreas, central nervous system, kidney, bladder, skin, epithelial appendage[[s]], breast tissue[[-]] or mammary gland[[s]], adipose fat tissue, and mucosal surfaces including oral mucosa, esophageal mucosa, vaginal mucosa and anal mucosa.

1

78. (currently amended): A therapeutic method for restoring organ, tissue or cellular function to a host mammal mammalian animal in need thereof, comprising the steps of:

- (a) isolating mesenchymal connective tissue-derived stem cells from a mammalian donor by culturing a tissue said-biopsy in the presence of medium that comprises at least 25% serum (v/v);
- (b) expanding [[a]] mesenchymal connective tissue-derived stem cells <u>isolated in (a)</u> to form an expanded population of undifferentiated cells; and
- (c) administering the expanded, <u>undifferentiated</u> cells to the <u>host mammalian animal</u>, <u>thereby restoring wherein organ</u>, tissue or cellular function is restored.
- 79. (currently amended): A method according to claim 78, wherein the function being restored is an enzymatic function.
- 80. (currently amended): A method according to claim 78, wherein the function being restored is genetic function.
- 81. (currently amended): A method according to claim 78, wherein the mammalian-donor and the host are is the same individual patient.
- 82. (currently amended): A method according to any one of claims claim 78 to 81, wherein the function being restored is a function of an organ, tissue or cell [[is]] selected from the group consisting of bone marrow, blood, spleen, liver, lung, intestinal tract, eye, brain, immune system, bone, connective tissue, muscle, heart, blood vessel[[s]], pancreas, central nervous system, peripheral nervous system, kidney, bladder, skin, epithelial appendages, breast or [[-]] mammary gland[[s]], adipose fat tissue, and mucosal surfaces including oral mucosa, esophageal mucosa, vaginal mucosa and anal mucosa.

83. (currently amended): A method of inhibiting the rejection by a host mammal of transplanted donor [[a]] heterologous mesenchymal connective tissue-derived stem cells transplanted into a patient, comprising the steps of:

- (a) modifying said donor stem cells before transplantation by introducing <u>ex vivo</u>, into a mesenchymal connective tissue-derived stem cell according to claim 20, <u>ex vivo</u>, a nucleic acid sequence encoding the <u>host's recipient's-MHC</u> antigens operably linked to a promoter, <u>so that wherein</u> the <u>encoded MHC</u> antigens are expressed by the <u>mesenchymal connective tissue-derived</u> stem cells; and
- (b) transplanting the <u>modified mesenchymal connective tissue derived stem cells of (a)</u> into the <u>host patient</u>,

wherein the host's MHC antigens are expressed on said stem cells at a level sufficient to inhibit immune recognition and the rejection of the transplanted mesenchymal connective tissue derived stem cells.

- 84. (currently amended): A method according to claim 83, wherein the stem cell donor and the host patient is are members of the same or different species or another mammalian species as the donor of the mesenchymal connective tissue-derived stem cells.
- 85. (currently amended): A method according to claim 83, wherein the mesenchymal connective tissue-derived-stem cells are transplanted into the host patient via by localized-injection, systemic injection, parenteral administration, or oral administration, or by intrauterine injection into an embryo.
- 86. (currently amended): A method according to claim 85, wherein <u>said</u> localized injection <u>administration is via comprises</u>-catheter-administration.
- 87. (currently amended): A method according to any one of claims claim 83 to 86, wherein the cells are transplanted in conjunction with a pharmaceutically acceptable matrix.
- 88. (original): A method according to claim 87, wherein the matrix is biodegradable.
- 89. (currently amended): A method of nuclear transfer comprising the step of transferring a mesenchymal connective tissue-derived stem cell according to claim 20 or a nucleus nuclei isolated therefrom said mesenchymal connective tissue derived stem cell into an enucleated oocyte.

7

90. (currently amended): A method for producing a genetically engineered or transgenic <u>oocyte</u> capable of developing into a genetically engineered or transgenic non-human mammal, the method comprising:

- (a) inserting a selected gene into, removing a selected gene from, or modifying a selected desired gene in, a mesenchymal connective tissue-derived stem cell according to claim 20 or in a nucleus nuclei isolated therefrom said mesenchymal connective tissue-derived stem cell to produced a genetically modified cell or nucleus; and
- (b) transferring said <u>modified</u> <u>mesenchymal connective tissue derived stem-cell or</u> <u>nucleus nuclei</u> into an enucleated oocyte,

thereby producing said oocyte.

- 91. *(currently amended):* A method for producing a genetically engineered or transgenic non-human mammal comprising:
 - (a) inserting a selected gene into, removing a selected gene from, or modifying a selected desired gene in, a mesenchymal connective tissue-derived non-human mammalian stem cell according to claim 20 or in a nucleus nuclei isolated therefrom a mesenchymal connective tissue-derived stem cell isolated from a non-human mammal; and
 - (b) inserting said mesenchymal connective tissue derived stem cell or nuclei nucleus into an enucleated oocyte under conditions suitable for the formation of a reconstituted oocyte-cell;
 - (c) activating the reconstituted <u>oocyte eell</u>-to form an embryo;
 - (d) culturing said embryo until <u>it reaches a developmental stage beyond greater than the a</u>

 2-cell developmental stage; and
 - (e) transferring said cultured embryo to a host mammal such that the embryo develops into a genetically engineered or transgenic fetus and is subsequently born.

92. (currently amended): A method for cloning a non-human mammal comprising:

- (a) inserting a mesenchymal connective tissue-derived stem cell according to claim 20 or a nucleus nuclei isolated therefrom said mesenchymal connective tissue derived stem cell into an enucleated mammalian oocyte, under conditions suitable for the formation of a reconstituted oocyte cell;
- (b) activating the reconstituted <u>oocyte</u> cell to form an embryo;
- (c) culturing said embryo until <u>it reaches a developmental stage beyond greater than the a</u>

 2-cell developmental stage; and
- (d) transferring said cultured embryo to an appropriate female host mammal such that the embryo develops into a fetus and is subsequently born.